

Cancer cells produce high levels of reactive oxygen species (ROS) that lead to a state of increased basal oxidative stress (Martin-Cordero et al., 2012). Subsequently, this state of oxidative stress makes cancer cells vulnerable to agents that further increase ROS levels, thus the use of pro-oxidant mediators is emerging as an exciting strategy to selectively target tumor cells. Natural products have provided a significant contribution to the development of several drugs used in cancer chemotherapy as standard treatment (Martin-Cordero et al., 2012). Recent data suggests that ROS participate in the anticancer activity of many chemotherapeutic agents commonly used in the clinic, including paclitaxel, docetaxel, cisplatin, doxorubicin, arsenic trioxide, bortezomib, procarbazine and etoposide (Martin-Cordero et al., 2012). The literature also revealed that many natural products are available as chemo-preventive agents against commonly occurring cancer types. About 60% of currently used anticancer agents are obtained from natural sources, including plants and microorganisms. Mycotoxins (fungal toxins) though known to be toxic to the animal and human systems still find their use in therapeutic application. Tricothecenes showed antitumor activities in different types of cancer cell line and in vivo. (Sagar Naskar et al., 2015). As indicated, a variety of tricothecene mycotoxins function by inducing ribotoxic stress. Moon and Pestka (Moon and Pestka, 2002) report that deoxynivalenon (DON), a common tricothecene agricultural contaminant produced by *Fusarium graminearum* and *Fusarium culmorum*, is a potent inducer of Ribotoxic stress (Laskin et al., 2002). At the cellular level DON interacts with the peptidyltransferase at the 60S ribosomal subunit levels" (Pestka, 2008). As a result, protein synthesis is impaired, but also a so called "ribotoxic stress syndrome" is induced, resulting in the activation of the mitogen-activated protein kinases (MAPKs) and their down-stream pathways covering apoptosis (Laskin et al., 2002; Shifrin and Anderson, 1999). The effects of DON on cellular physiology are complex and depend on the tested DON concentration and cell type (Li et al., 2014). In this project we will evaluate common tricothecene - DON as a potential apoptosis inducer in PCa cells via activating ROS-dependent ER stress and mitochondrial pathways. Moreover, we will check DON contribution in dysregulation of intratumoral steroid hormone synthesis. The advantage that makes prospective is the possibility that DON can be used in conjunction with TRAIL as a potent TRAIL sensitizer for synergistic apoptosis induction via production of ROS and downregulation of steroids in prostate cancer cells. Our study assumes that ROS production could be an important target for developing new anti-cancer drugs.

References

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